

# **Non–Hodgkin Lymphoma and Occupational Exposure to Agricultural Pesticide Chemical Groups and Active Ingredients: A Systematic Review and Meta–Analysis**

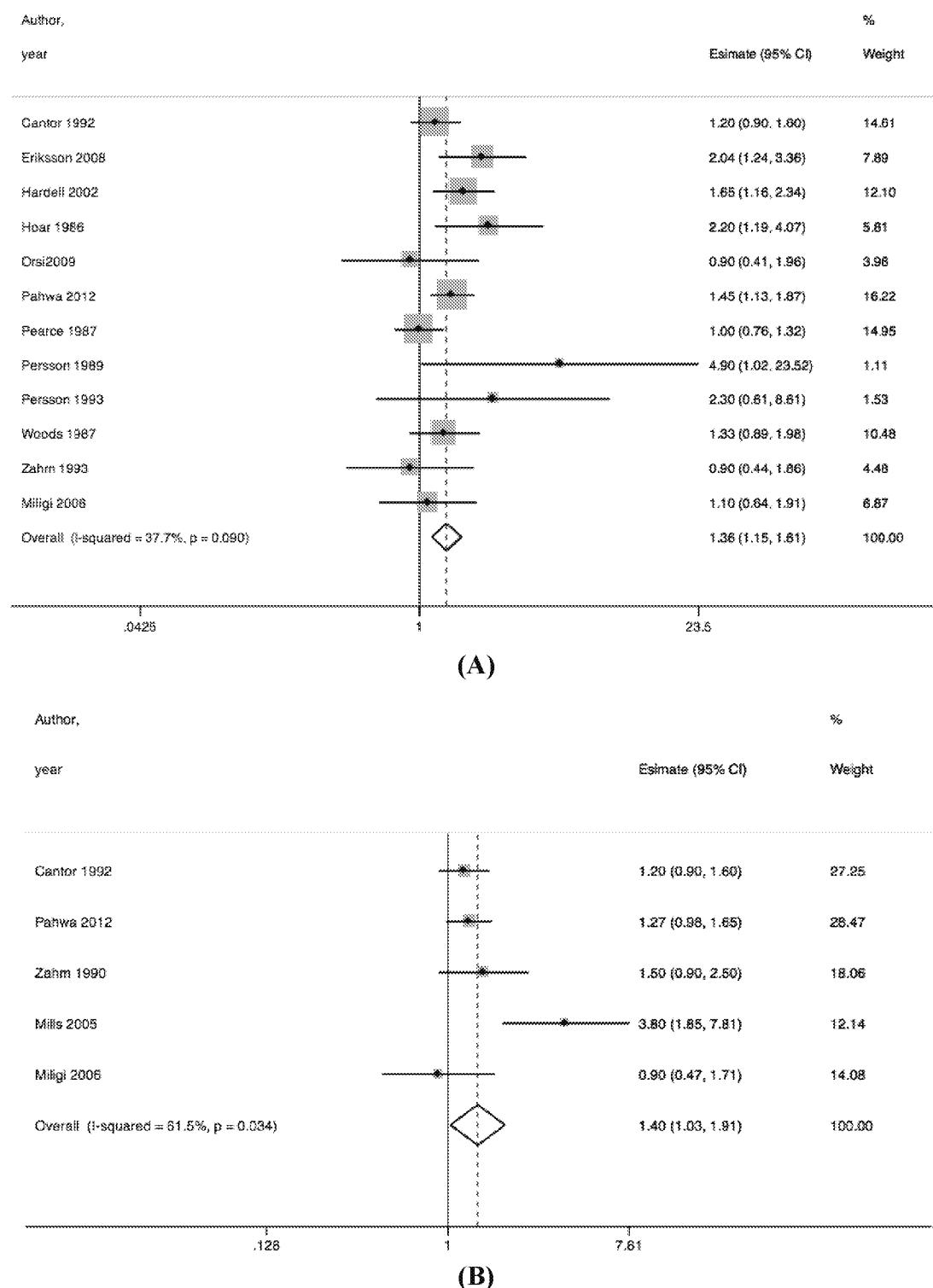
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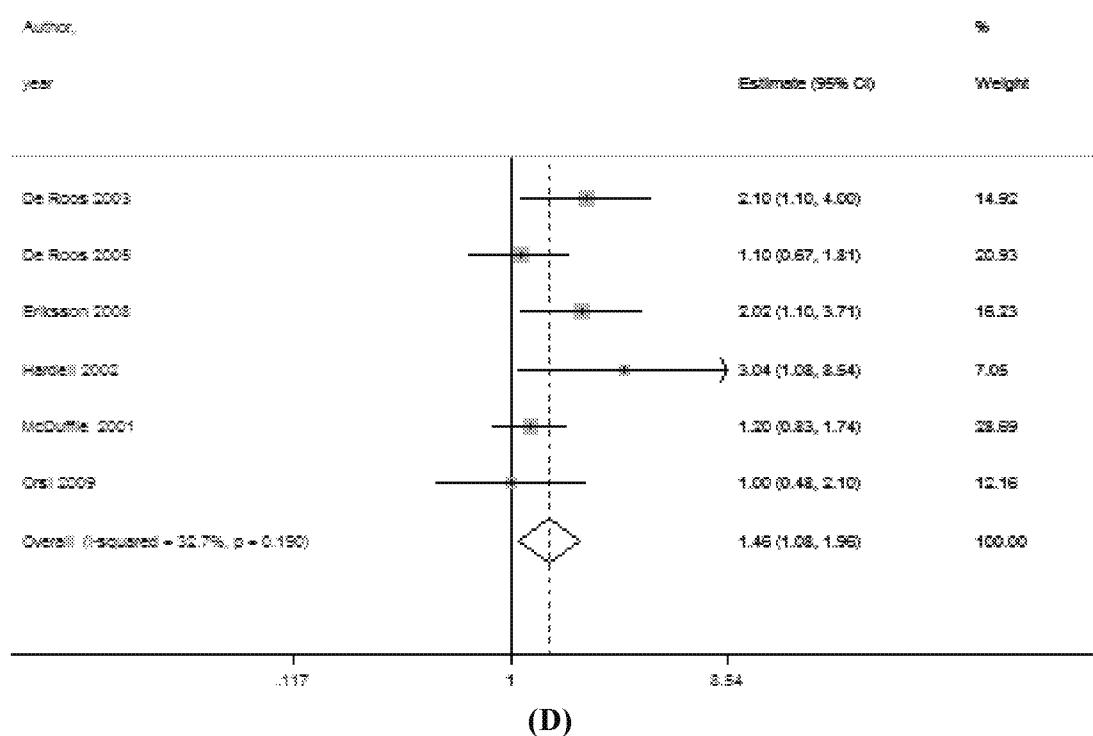
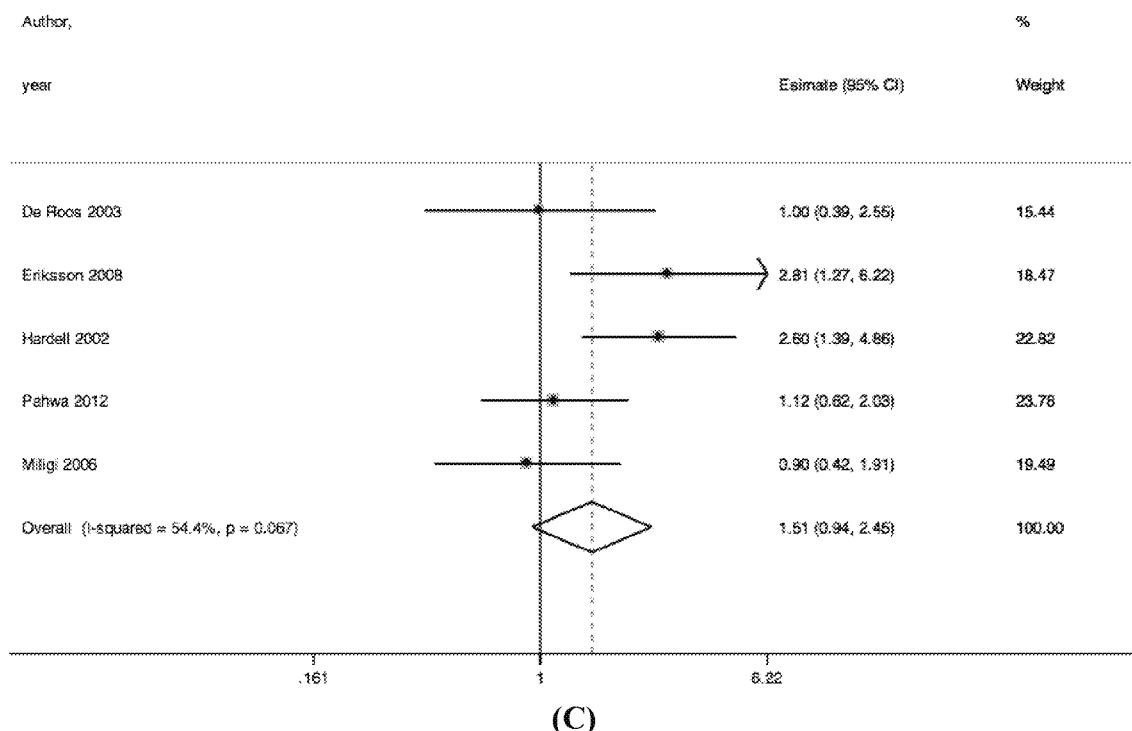
## **S1. List of terms included in the PubMed literature search.**

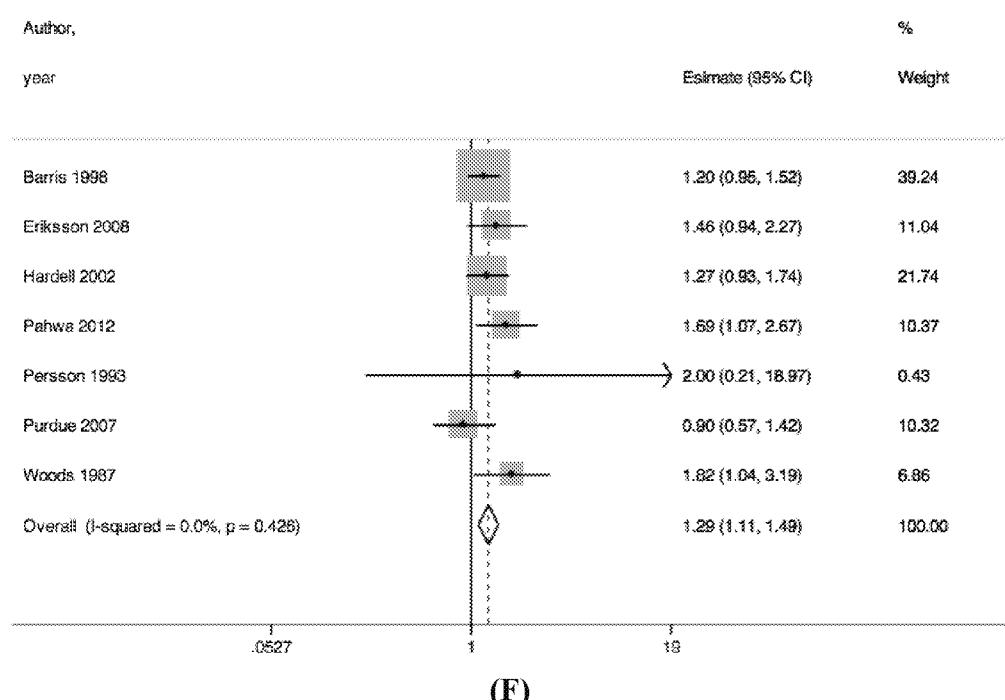
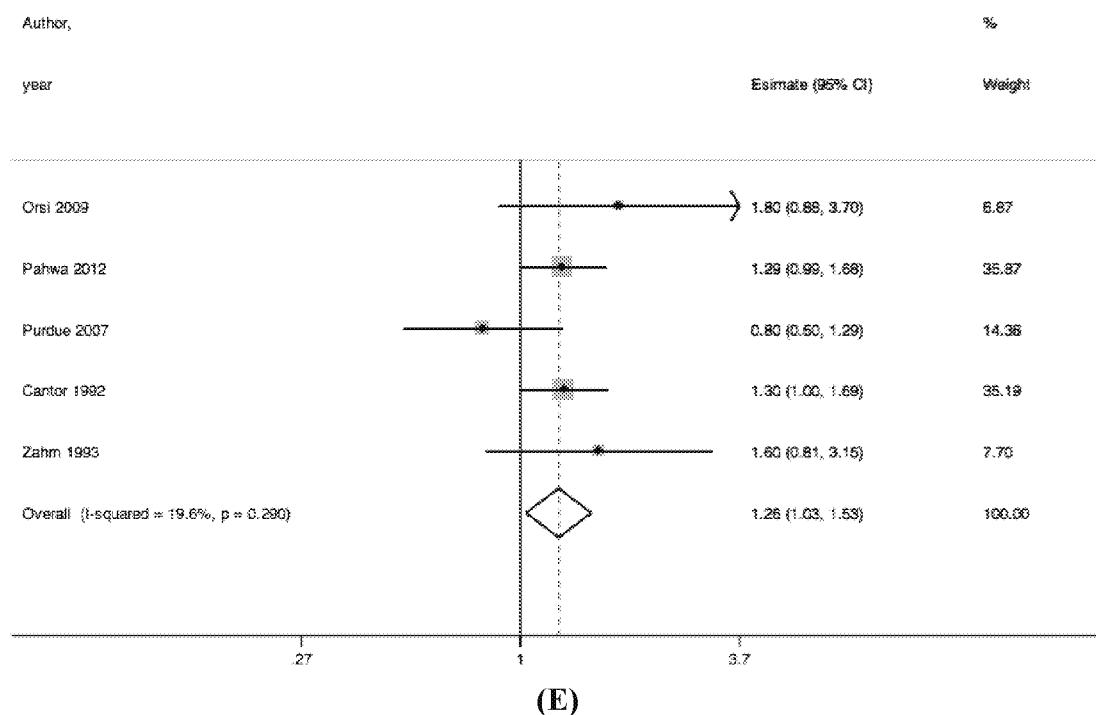
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OR "pesticides"[MeSH Terms] OR pesticides[nm] OR (insecticid[tiab] OR insecticidal[tiab]  
OR insecticidal/acaricidal[tiab] OR insecticidal/anthelmintic[tiab] OR  
insecticidal/antifeedant[tiab] OR insecticidal/irritant[tiab] OR insecticidal/larvicidal[tiab] OR  
insecticidal/narcotic[tiab] OR insecticidal'[tiab] OR insecticidal'b[tiab] OR insecticidally[tiab]  
OR insecticidation[tiab] OR insecticide[tiab] OR insecticide/acaricide[tiab] OR  
insecticide/antifeedant[tiab] OR insecticide/ascaricide[tiab] OR insecticide/atrazine[tiab] OR  
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insecticide/nematocide[tiab] OR insecticide/organophosphorus[tiab] OR  
insecticide/pesticide/herbicide[tiab] OR insecticide/repellant[tiab] OR  
insecticide/repellent[tiab] OR insecticide'[tiab] OR insecticide's[tiab] OR insecticided[tiab] OR  
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insecticides/acaricides[tiab] OR insecticides/attract[tiab] OR insecticides/larvicides[tiab] OR  
insecticides/mn[tiab] OR insecticides/pesticides[tiab] OR insecticides/repellents[tiab] OR  
insecticides'[tiab] OR insecticidetreated[tiab] OR insecticidewise[tiab] OR insecticidial[tiab]  
OR insecticidic[tiab] OR insecticiding[tiab] OR insecticity[tiab] OR insecticido[tiab]) OR  
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OR herbicide[tiab] OR herbicide/binding[tiab] OR herbicide/dessicant[tiab] OR  
herbicide/fungicide[tiab] OR herbicide/g[tiab] OR herbicide/humic[tiab] OR  
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OR herbicide/mutation[tiab] OR herbicide/nematicide[tiab] OR herbicide/outcome[tiab] OR  
herbicide/pesticide[tiab] OR herbicide/substrate[tiab] OR herbicide/therapeutic[tiab] OR  
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AND "humans"[MeSH Terms])) NOT News[Publication Type]) NOT Congresses[Publication  
Type]) NOT Review[Publication Type]) AND ("1980/01/01"[PDAT] : "2013/06/31"[PDAT])  
AND "humans"[MeSH Terms]) NOT "child"[MeSH Terms] AND ((("1980/01/01"[PDAT] :  
"2013/12/31"[PDAT]) AND "humans"[MeSH Terms]))

**Figure S1.** Forest plots showing estimates of association between non-Hodgkin lymphoma and occupational, agricultural exposures to (A) phenoxy herbicides, (B) 2,4-D, (C) MCPA, (D) glyphosate, (E) organochlorine insecticides, and (F) DDT.



**Figure S1. Cont.**

**Figure S1. Cont.**

Notes: 2,4-D, 2,4-Dichlorophenoxyacetic acid; 2,4,5-T, 2,4,5-Trichlorophenoxyacetic acid; DDT, dichlorodiphenyltrichloroethane; MCPA, 2-methyl-4-chlorophenoxyacetic acid.

**Table S1.** Results of the sensitivity analysis of the effects of gender on the meta-analytic relative risk estimates of association between non-Hodgkin lymphoma and occupational exposure to agricultural pesticides

Chemical	Meta relative risk, 95% CI	I <sup>2</sup>	Papers contributing
<b>Male only population</b>			
Amide herbicides	1.7, 0.7–3.8	64.0%	[1,2]
Glyphosate	1.7, 1.0–2.9	52.7%	[3–5]
Phenoxy herbicides	1.4, 1.1–1.6	44.1%	[1,2,4,6–8]
2,4-D	1.3, 1.2–1.5	0.0%	[1,6,9]
MCPA	1.5, 0.8–2.7	56.6%	[3,4,6]
Benzoic acid herbicides	1.3, 0.9–1.9	0.0%	[1,2]
Trifluralin	1.0, 0.6–1.5	0.0%	[3,5]
Triazine herbicides	1.5, 0.70–3.4	73.5%	[1,2]
OP insecticides	1.7, 1.3–2.1	39.2%	[6,10]
Diazinon	1.7, 1.2–2.3	0.0%	[5,10]
Malathion	1.8, 1.4–2.2	0.0%	[6,10]
Carbamate insecticides	1.8, 1.3–2.4	0.0%	[5,11]
OC insecticides	1.3, 1.1–1.6	0.0%	[1,6]
DDT	1.3, 1.1–1.5	27.3%	[4,6,8,12]
Aldrin	1.4, 0.2–11.1	92.0%	[3,5]
Chlordane	1.3, 0.9–1.7	0.0%	[3,5,8]
Lindane	1.9, 1.2–2.9	38.0%	[5,13,14]
<b>Male and female population</b>			
Phenoxy herbicides	1.6, 1.0–2.5	42.2%	[15–19]
2,4-D	1.8, 0.5–7.5	88.3%	[19,20]
MCPA	1.6, 0.5–4.8	76.0%	[15,19]
OC insecticides	1.2, 0.5–2.5	70.4%	[16,21]
DDT	1.2, 0.8–1.7	18.0%	[15,18,21]

Notes: 2,4-D, 2,4-Dichlorophenoxyacetic acid; DDT, dichlorodiphenyltrichloroethane; MCDA, 2-methyl-4-chlorophenoxyacetic acid; NHL, OC, Organochlorine; OP; Organophosphorus.

**Table S2.** Results of the sensitivity analysis of the effects of study design on the meta-analytic relative risk estimates of association between non-Hodgkin lymphoma and occupational exposure to agricultural pesticides, with contributing estimates restricted to case-control studies.

Chemical	Meta relative risk, 95% CI	I <sup>2</sup>	Paper contributing
Glyphosate	1.6, 1.1–2.2	36.6%	[3–5,15,16]
Organochlorine insecticides	1.3, 1.1–1.6	0.0%	[1,6,16,22]
Aldrin	1.4, 0.2–11.1	92.0%	[3,5]
Chlordane	1.3, 0.9–1.7	0.0%	[3,5,8]
DDT	1.3, 1.1–1.6	0.0%	[4,6,8,12,15,18]
Lindane	1.9, 1.2–2.9	38.0%	[5,13,14]

Notes: DDT; dichlorodiphenyltrichloroethane.

**Table S3.** Results of the sensitivity analysis of the effects of diagnosis period on the meta-analytic relative risk estimates of association between non-Hodgkin lymphoma and occupational exposure to agricultural pesticides

Chemical	Meta relative risk, 95% CI	I <sup>2</sup>	Papers contributing
<b>Diagnosis period 1975–1989</b>			
2,4-D	1.8, 1.0–3.1	76.6%	[1,9,20]
Amide herbicides	1.4, 0.8–2.3	43.2%	[1,2,22]
Glyphosate	2.3, 1.4–4.0	0.0%	[3,4]
MCPA	1.7, 0.7–4.4	63.8%	[3,4]
Phenoxy herbicides	1.4, 1.1–1.7	44.9%	[1,2,4,7,8,17,18,22]
Triazine herbicides	1.4, 0.9–2.2	47.3%	[1,2,23]
Carbamate insecticides	1.6, 1.1–2.4	0.0%	[11,22]
OC insecticides	1.3, 1.0–1.7	0.0%	[1,22]
OP insecticides	1.5, 1.2–1.8	0.0%	[10,22]
Diazinon	1.6, 1.2–2.2	0.0%	[10,20]
Chlordane	1.5, 1.0–2.5	0.0%	[3,8]
Trifluralin	0.9, 0.6–1.3	0.0%	[3,20,22]
Malathion	1.6, 1.3–2.1	0.0%	[10,20]
DDT	1.3, 1.1–1.5	0.0%	[4,8,12,18]
Lindane	2.0, 0.9–4.4	65.0%	[13,14]
<b>Diagnosis period in the 1990s</b>			
2,4-D	1.6, 0.8–3.1	79.3%	[6,19,20]
Glyphosate	1.5, 1.0–2.1	41.1%	[4,5,15,24]
MCPA	1.6, 0.9–2.9	61.9%	[4,6,15,19]
Phenoxy herbicides	1.5, 1.3–1.8	0.5%	[4,6,15,19]
Trifluralin	1.0, 0.6–1.6	0.0%	[5,20]
Aldrin	1.5, 0.2–10.1	90.0%	[5,21]
Chlordane	0.9, 0.6–1.4	42.2%	[5,21]
Diazinon	1.5, 1.0–2.4	0.0%	[5,20]
DDT	1.3, 1.0–1.6	25.4%	[4,6,15,21]
Lindane	1.9, 1.1–3.2	46.6%	[5,14,21]
Malathion	1.9, 1.5–2.5	0.0%	[6,20]
OC insecticides	1.1, 0.7–1.7	66.2%	[6,21]
<b>Diagnosis period in the 2000s</b>			
Glyphosate	1.3, 0.9–2.0	31.8%	[15,16,24]
Phenoxy herbicides	1.4, 0.7–3.2	66.7%	[15,16]
Lindane	2.0, 0.8–5.0	70.6%	[14, 21]
OC insecticides	1.2, 0.5–2.5	70.4%	[16,21]

Notes: 2,4-D, 2,4-Dichlorophenoxyacetic acid; DDT, dichlorodiphenyltrichloroethane; MCPA, 2-methyl-4-chlorophenoxyacetic acid; NHL, OC, Organochlorine; OP, Organophosphorus;

<sup>1</sup>The first, second, and third editions of the International classification of diseases for oncology were introduced in 1976, 1990, and 2000, respectively.

**Table S4.** Results of the sensitivity analysis of the effects of geographic region on the meta-analytic relative risk estimates of association between non Hodgkin lymphoma and occupational exposure to agricultural pesticides

Chemical	Meta risk ratio estimate, 95% CI	$I^2$	Papers contributing
<b>Only papers that report results from studies conducted in North America</b>			
Glyphosate	1.3, 1.0–1.8	26.7%	[3,5,24]
Phenoxy herbicides	1.4, 1.1–1.6	12.9%	[1,2,6,8,22]
2,4-D	1.5, 1.1–2.1	66.5%	[1,6,9,20]
MCPA	1.1, 0.7–1.8	0.0%	[3,6]
DDT	1.3, 1.0–1.7	45.1%	[6,8,12,21]
OC insecticides	1.2, 1.0–1.5	24.7%	[1,6,21,22]
OP insecticides	1.6, 1.3–2.0	15.1%	[6,10,22]
Lindane	1.5, 1.2–1.9	0.0%	[5,13,21]
<b>Only papers that report results from studies conducted in the United States</b>			
2,4-D	1.8, 1.0–3.1	76.6%	[1,6,9,20]
Amide herbicides	1.4, 0.8–2.3	43.2%	[1,2,22]
Glyphosate	1.5, 0.8–2.8	58.5%	[3,24]
Phenoxy herbicides	1.3, 1.0–1.7	27.1%	[1,2,8,22]
Trifluralin	0.9, 0.6–1.3	0.0%	[3,20,22]
Triazine herbicides	1.4, 0.9–2.2	47.3%	[1,2,22]
Aldrin	0.5, 0.4–0.8	0.0%	[3,21]
Carbamate insecticides	1.6, 1.1–2.4	0.0%	[22,23]
Chlordane	1.1, 0.7–2.0	55.0%	[3,8,21]
DDT	1.2, 0.9–1.7	44.8%	[8,12,21]

**Table S4. Cont.**

Chemical	Meta risk ratio estimate, 95% CI	I <sup>2</sup>	Papers contributing
<b>Only papers that report results from studies conducted in the United States</b>			
Diazinon	1.6, 1.2–2.2	0.0%	[10,20]
Lindane	1.4, 1.1–1.9	0.0%	[13,21]
Malathion	1.6, 1.3–2.1	0.0%	[10,20]
OC insecticides	1.2, 0.8–1.7	47.5%	[1,21,22]
OP insecticides	1.5, 1.2–1.8	0.0%	[10,22]
<b>Only papers that report results from studies conducted in European countries</b>			
Glyphosate	1.7, 1.0–3.1	42.8%	[4,15,16]
Phenoxy herbicides	1.6, 1.2–2.1	29.1%	[4,15–19]
MCPA	1.9, 0.9–3.8	64.8%	[4,15,19]
<b>Only papers that report results from studies conducted in Sweden</b>			
Glyphosate	2.2, 1.3–3.8	0.0%	[4,15]
MCPA	2.7, 1.6–4.4	0.0%	[4,15]
Phenoxy herbicides	1.9, 1.4–2.4	0.0%	[4,15,17,18]
DDT	1.3, 1.0–1.7	0.0%	[4,15,18]

Notes: 2,4-D, 2,4-Dichlorophenoxyacetic acid; DDT, dichlorodiphenyltrichloroethane; MCPA, 2-methyl-4-chlorophenoxyacetic acid; NHL, OC, Organochlorine; OP, Organophosphorus

**Table S5.** Results of the sensitivity analysis of the effects of control source on the meta-analytic relative risk estimates of association between non-Hodgkin lymphoma and occupational exposure to agricultural pesticides, with contributing estimates restricted to those from population-based case-control studies.

Chemical	Meta risk ratio estimate, 95% CI	I <sup>2</sup>	Papers contributing
<b>HERBICIDES</b>			
Amide herbicides	1.4, 0.8–2.3	43.2%	[1,2,22]
Glyphosate	1.7, 1.2–2.6	39.0%	[3,4,5,15]
Phenoxy herbicides	1.5, 1.2–1.7	20.7%	[1,2,4,6,8,15,17–19,22]
Triazine herbicides	1.4, 0.9–2.2	47.3%	[1,2,22]
<b>INSECTICIDES</b>			
Organochlorine insecticides	1.2, 1.0–1.5	24.7%	[1,6,21,22]
Organophosphate insecticides	1.6, 1.4–1.8	0.0%	[1,6,10,22]

**Table S6.** Results of the sensitivity analysis of the effects of paper contributing on the meta-analytic relative risk estimates of association between non-Hodgkin lymphoma and occupational exposure to agricultural pesticides.

Chemical	Meta estimate, 95% CI	I <sup>2</sup>	Change	Papers contributing
<b>HERBICIDES</b>				
Alachlor	0.9, 0.6–1.5	69.7%	Use Cantor 1992 [1] instead of De Roos 2003 [3]	[1,25]
Glyphosate	1.3, 1.0–1.7	18.2%	Use Cantor 1992 [1] instead of De Roos 2003 [3]	[1,24]
2,4-D	1.3, 0.8–2.1	82.5%	Use De Roos 2003 [3] instead of Cantor 1992 [1] and Zahm 1990 [9]	[3,6,19,20]
Carbamate herbicides	1.2, 0.5–2.6	24.8%	Use Cantor 1992 [1] and Hoar 1986 [2] instead of Zheng 2001 [11]	[1,2,16,22]
Trifluralin	1.1, 0.7–1.8	40.0%	Use Cantor 1992 [1] and Hoar 1986 [2] instead of De Roos 2003[3]	[1,2,5,20,22]
<b>INSECTICIDES</b>				
OP insecticides	1.7, 1.4–2.0	0.0%	Use Cantor 1992 [1] instead of Waddell 2001 [10]	[1,6,16,22]
Diazinon	1.5, 1.1–2.1	0.0%	Use Cantor 1992 [1] instead of Waddell 2001 [10]	[1,3,5,20]
Diazinon	1.7, 1.2–2.4	0.0%	Use De Roos 2003 [3] instead of Cantor 1992 [1] and instead of Waddell 2001 [10]	[3,5,20]
Dimethoate	1.2, 0.7–2.0	0.0%	Use De Roos 2003 [3] instead of Waddell 2001 [10]	[3,5]
Malathion	1.7, 1.3–2.2	13.5%	Use Cantor 1992 [1] (use of malathion on animals) instead of Waddell 2001 [10] or De Roos 2003 [3]	[1,6,20]
Malathion	1.8, 1.4–2.4	0.0%	Use Cantor 1992 [1] (use of malathion on crops) instead of Waddell 2001 [10] or De Roos 2003 [3]	[1,6,20]
Malathion	1.6, 1.2–2.3	37.2%	Use De Roos 2003 [3] instead of Waddell 2001 [10] and Cantor 1992 [1]	[3,6,20]
Carbaryl	1.9, 1.3–2.9	0.0%	Use Cantor 1992 [1] instead of Zheng 2001 [11]	[1,5]
Carbaryl	1.5, 0.7–3.1	64.7%	Use De Roos 2003 [3] instead of Cantor 1992 [1] or Zheng 2001 [11]	[3,5]
Carbofuran	1.1, 0.7–1.8	0.0%	Use Cantor 1992 [1] instead of Zheng 2001 [11]	[1,5]

Table S6. Cont.

Chemical	Meta estimate, 95% CI	I <sup>2</sup>	Change	Papers contributing
Carbofuran	1.1, 0.6–2.0	23.0%	Use De Roos 2003 [3] instead of Cantor 1992 [1] or Zheng 2001 [11]	[3,5]
DDT	1.3, 1.1–1.5	0.0%	Use Cantor 1992 [1] (use of DDT on animals) instead of Baris 1998 [12]	[1,4,6,8,15,18,21]
DDT	1.3, 1.2–1.6	9.1%	Use Cantor 1992 [1] (use of DDT on crops) instead of Baris 1998 [12]	[1,4,6,8,15,18,21]
Methoxychlor	1.0, 0.8–1.4	0.0%	Use Cantor 1992 [1] instead of De Roos 2003 [3]	[1,5]
Aldrin	1.3, 0.5–2.9	80.2%	Use Cantor 1992 [1] instead of De Roos 2003 [3]	[1,5,21]
Chlordane	1.2, 0.8–1.7	48.7%	Use Cantor 1992 [1] (Use of chlordane on animals) instead of De Roos 2003 [3]	[1,5,8,21]
Chlordane	1.1, 0.8–1.7	42.1%	Use Cantor 1992 [1] (Use of chlordane on crops) instead of De Roos 2003 [3]	[1,5,8,21]
Dieldrin	1.0, 0.4–2.2	50.8%	Use Cantor 1992 [1] instead of De Roos 2003 [3]	[1,21]
Heptachlor	1.0, 0.7–1.7	20.5%	Use Cantor 1992 [1] instead of De Roos 2003 [3]	[1,21]
Lindane	1.62, 1.16–2.27	30.6%	Use Cantor 1992 [1] (use of lindane on animals) instead of Blair 1998 [13] and De Roos 2003 [3]	[1,5,14,21]
Lindane	1.85, 1.27–2.69	23.30 %	Use Cantor 1992 [1] (use of lindane on crops) instead of Blair 1998 [13] and De Roos 2003 [3]	[1,5,14,21]
Lindane	1.62, 1.08–2.41	39.20 %	Use De Roos 2003 [3] instead of Cantor 1992 [1] or Blair 1998 [13]	[3,5,14,21]
Toxaphene	1.25, 0.72–2.19	23.50 %	Use Cantor 1992 [1] (use of toxaphene on animals) instead of De Roos 2003 [3]	[1,20,21]
Toxaphene	1.50, 0.96–2.33	0.00%	Use Cantor 1992 [1] (use of toxaphene on crops) instead of De Roos 2003 [3]	[1,20,21]

Notes: 2,4-D, 2,4-Dichlorophenoxyacetic acid; DDT, dichlorodiphenyltrichloroethane; MCPA, 2-methyl-4-chlorophenoxyacetic acid; NHL, OC, Organochlorine; OP, Organophosphorus.

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